Ebola virus disease causes severe hemorrhagic fever, with a case-fatality rate of 50% to 90% (1). The ongoing epidemic in West Africa is the largest Ebola outbreak ever recorded and is rapidly crossing borders. The relentless epidemiologic trajectory and geographic dissemination represent a public health crisis that shows no signs of diminishing under current efforts. We believe that the time to deploy Ebola vaccines is now, as advocated in recent statements by the World Health Organization.

Ebola arises sporadically via zoonosis from fruit bats (the natural reservoir) to humans, often through great apes. Human-to-human transmission occurs primarily through contact with infected body fluids. This transmission route puts health care workers, family members, and persons preparing bodies for traditional funerals at high risk for the disease (1). Although no Ebola vaccines are currently licensed, many candidates have been developed in the past decade. A DNA vaccine has been shown to be safe and immunogenic in a phase 1 clinical trial (2). In addition, a therapeutic vaccine based on recombinant vesicular stomatitis viruses (rVSVs) expressing Ebola virus surface glycoprotein was found to confer prophylactic and postexposure protection in nonhuman primates (3). Despite the promise of these and other Ebola vaccine candidates, none have advanced to late-stage human trials and licensure. The challenge in this process has been the inability to evaluate vaccine efficacy in human populations given the sporadic nature of Ebola outbreaks.

For unique circumstances, such as those where conventional efficacy trials are not feasible, the U.S. Food and Drug Administration has created the “animal rule,” which states that licensure can be approved on the basis of animal model studies that replicate human disease combined with safety and immunologic data from humans (4). Nonhuman primates serve as the gold standard for animal models of disease transmission and protect health care workers, thus enabling an effective medical and epidemiologic response. Epidemiologic modeling can facilitate the optimization of such vaccination strategies when vaccine supply is limited and production has to be scaled up. Primarily, an Ebola vaccine could mitigate disease transmission and protect health care workers, thus enabling an effective medical and epidemiologic response in affected areas. Secondarily, the emergency deployment of an Ebola vaccine may also serve as a source of data that could be used to further demonstrate efficacy and waning properties that are fundamental to informing preparedness strategies to prevent future outbreaks.

Vaccination alone is no panacea. Cultural and socioeconomic factors and suspicion of Western medical approaches complicate all medical interventions. Epidemiologic practices, such as trace-back investigations to identify...
and quarantine persons exposed to Ebola, are pivotal to controlling spread. Such control methods require trained personnel on the ground in even the most remote locations. Given that nosocomial transmission has contributed substantially to past Ebola outbreaks (1), it is also imperative to integrate vaccination with nosocomial contact precautions and quarantining.

Although vaccine production, transport, and cost are undeniable logistical challenges to any vaccination strategy, the resources required to implement vaccination should be made available by the international community given the magnitude of the threat that the current Ebola outbreak poses to countries in which transmission is occurring and to which it may spread. Even from a pragmatic perspective, it is in the interest of the international community to assist West Africa in containing the Ebola outbreak. Curtailing an outbreak is always easier in its earliest stages than after it has disseminated geographically. That window of opportunity may be rapidly closing.

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Grant Support: By the National Institutes of Health (NIH 2 U01 GM087719 and 5 U01 GM105627).

Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M14-1904.

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### Table. Viable Ebola Vaccine Candidates

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Properties</th>
<th>Vaccination Scenario</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>rVSV + ZEBOV-GP</td>
<td>Trials in NHPs elicited immunogenic response against lethal and aerosol challenge. Conveyed protection in Ebola-exposed and immunocompromised NHPs.</td>
<td>Suited for outbreak response, including postexposure prophylaxis. Also appropriate for use in immunocompromised populations, such as those with a high prevalence of HIV.</td>
<td>3, 7</td>
</tr>
<tr>
<td>rRABV + ZEBOV-GP</td>
<td>Trials in NHPs elicited immunogenic response against lethal challenge.</td>
<td>Suited for human and wildlife vaccination. Dual RABV/EBOV vaccine may be more acceptable in endemic areas.</td>
<td>8</td>
</tr>
<tr>
<td>DNA + rAd5 + ZEBOV-GP, rAd5 + ZEBOV-GP</td>
<td>Trials in NHPs elicited immunogenic response against lethal challenge.</td>
<td>Preparedness strategies for health care workers and high-risk populations.</td>
<td>2</td>
</tr>
<tr>
<td>Virus-like particles + ZEBOV-GP + ZEBOV-NP + ZEBOV-VP40</td>
<td>Virus-like particles can be produced in insect cells, making them suitable for large-scale production.</td>
<td>Preparedness strategies for health care workers and high-risk populations.</td>
<td>9</td>
</tr>
<tr>
<td>rHPIV3 + ZEBOV-GP</td>
<td>Trials in guinea pigs and NHPs elicited immunogenic response against lethal challenge. Potential for needle-free administration.</td>
<td>Preparedness strategies for health care workers and high-risk populations.</td>
<td>10</td>
</tr>
<tr>
<td>rCMV + ZEBOV-NP</td>
<td>Trials in mice elicited immunogenic response against lethal challenge. Highly species-specific.</td>
<td>Suited for great ape vaccination in endemic areas.</td>
<td>6</td>
</tr>
<tr>
<td>rEBOV subunit vaccine + TLR agonist</td>
<td>Trials in mice elicited immunogenic response against lethal challenge. Subunit vaccines stable for storage and delivery at ambient temperatures.</td>
<td>Suited for stockpiling and vaccine delivery.</td>
<td>5</td>
</tr>
</tbody>
</table>

GP = glycoprotein; NHP = nonhuman primate; NP = nucleoprotein; rAd5 = recombinant adenovirus serotype 5; rCMV = recombinant cytomegalovirus; rEBOV = recombinant Ebola virus; rHPIV3 = recombinant human parainfluenza virus type 3; rRABV = recombinant rabies virus; rSVS = recombinant vesicular stomatitis virus; TLR = Toll-like receptor; ZEBOV = Zaire ebolavirus.

### References


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Obtaining of funding: A.P. Galvani.
Administrative, technical, or logistic support: N. Wenzel.
Collection and assembly of data: N. Wenzel.